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ENCLOSURES (check all that apply)

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Signing Attorney/Agent (Reg. No.)	**CAROL L. FRANCIS, PH.D., 36,513** **BOZICEVIC, FIELD & FRANCIS, LLP**
Signature	
Date	**December 20, 2006**

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APPELLANT'S BRIEF

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Attorney Docket No.	DURE-023
Confirmation No.	9651
First Named Inventor	THEEUWES, FELIX
Application Number	09/917,181
Filing Date	July 26, 2001
Group Art Unit	1641
Examiner Name	LAM, ANN Y.
Title: "LOCAL CONCENTRATION MANAGEMENT SYSTEM"	

Sir:

This Brief is filed in support of Appellant's appeal from the Examiner's Final Rejection dated January 24, 2006. No claims have been allowed, and Claims 1, 2, 4, 6-13, 19-22, 24, 25 and 29-33 are pending. Claims 1, 2, 4, 6-13, 19-22, 24, 25 and 29-33 are appealed. A Notice of Appeal was filed on July 24, 2006.

The Board of Appeals and Interferences has jurisdiction over this appeal pursuant to 35 U.S.C. §134.

The Commissioner is hereby authorized to charge deposit account number 50-0815, reference no. DURE-023 to cover any fee required under 37 C.F.R. §1.17(b) for filing Appellant's brief. In the unlikely event that the fee transmittal or other papers are separated from this document and/or other fees or relief are required, Appellant petitions for such relief, including extensions of time, and authorizes the Commissioner to charge any fees under 37 C.F.R. §§ 1.16, 1.17 and 1.21 which may be required by this paper, or to credit any overpayment, to deposit account number 50-0815, reference no. DURE-023.

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REAL PARTY IN INTEREST

The inventors named on this patent application assigned their entire rights in the invention to Durect Corporation.

RELATED APPEALS AND INTERFERENCES

There are currently no other appeals or interferences known to Appellants, the undersigned Appellants' representative, or the assignee to whom the inventors assigned their rights in the instant case, which would directly affect or be directly affected by, or have a bearing on the Board's decision in the instant appeal.

STATUS OF CLAIMS

Claims 1, 2, 4, 6-13, 19-22, 24, 25 and 29-33 are rejected and are appealed herein.

Claims 3, 5, 14-18, 23 and 26-28 are canceled.

STATUS OF AMENDMENTS

No amendments to the Claims were filed subsequent to issuance of the Final Rejection.

SUMMARY OF CLAIMED SUBJECT MATTER

The invention relates to a medical device comprising an elongated body with a diffuser element that is both drug-permeable and water-permeable. The diffuser element allows the drug to be diluted prior to diffusing out of the diffuser element into the body of the subject. The device thus facilitates dilution of drug prior to delivery at a site in a patient's body, thereby reducing the local concentration of the agent released at the site. The device can thus mitigate toxicity, irritation and other

undesirable side effects that can result from exposure of tissue surrounding the delivery site to drug.

Claim 1 is directed a device comprising: an elongate body comprising a proximal end defining an inlet, and a distal end defining an outlet, the elongate body defining a lumen in the elongate body, said lumen extending between the proximal and distal ends (page 14, paragraph [0063], lines 1-6); and a diffuser element operatively associated with the elongate body so as to define a diffusion space, wherein the elongate body distal end outlet is disposed in and in fluid communication with the diffusion space (page 20, paragraph [0083], lines 1-5), and wherein the diffuser element is drug-permeable and water-permeable (page 22, paragraph [0090], lines 1-5) to provide for dilution of a drug in the diffusion space (page 20, paragraph [0083], lines 5-7).

Claim 2 is directed to the device of claim 1, wherein the diffuser element comprises a semipermeable membrane (page 23, paragraph [0091], lines 5-6), a microporous membrane (page 23, paragraph [0092], line 3) or an ion exchange membrane (page 23, paragraph [0092], lines 3-4).

Claim 4 is directed to the device of claim 1, wherein the distal outlet of the elongate body is defined by an exit orifice of a drug delivery device and the diffuser element is a cap in which the exit orifice is disposed (page 3, [paragraph 0008], lines 1-3).

Claim 6 is directed to the device of claim 1, wherein the diffusion space is defined by an outer wall of the elongate body and an inner wall of the diffuser element (page 10, paragraph [0047], lines 5-7).

Claim 7 is directed to the device of claim 1, wherein said diffuser element surrounds at least a portion of said elongate body (page 22, paragraph [0088], lines 1-2).

Claim 8 is directed to the device of claim 1, wherein the diffuser element is microporous (page 23, paragraph [0092], line 3).

Claim 9 is directed to the device of claim 1, wherein the diffuser element is a dense membrane (page 23, paragraph [0092], line 3).

Claim 10 is directed to the device of claim 1, wherein the diffuser element is an ion-exchange membrane (page 23, paragraph [0092], lines 3-4).

Claim 11 is directed to the device of claim 1, wherein a diffuser element distal end extends distally beyond the elongate body distal end (page 22, paragraph [0088], lines 4-5).

Claim 12 is directed to the device of claim 1, wherein the diffuser element is a ring-shaped element (page 22, paragraph [0088], lines 6-7).

Claim 13 is directed to the device of claim 1, wherein the diffuser element is selectively permeable to water (page 2, paragraph [0007], lines 9-11).

Claim 19 is directed to the device of claim 1, wherein the elongate body lumen is adapted for delivery of agent at a low volume rate (page 5, paragraph [0018], lines 1-4).

Claim 20 is directed to a drug delivery system comprising the device of claim 1 operably attached to a drug reservoir (page 4, paragraph [0011], lines 3-5).

Claim 21 is directed to the drug delivery system of claim 20, wherein the drug reservoir contains Baclofen (page 38, paragraph [0140], lines 1-2).

Claim 22 is directed to the drug delivery system of claim 20, wherein said drug is delivered in microliter or submicroliter quantities per day (page 5, paragraph [0018], lines 1-4).

Claim 24 is directed to the method of claim 25, wherein the formulation is introduced into the inlet at a low volume rate (page 5, paragraph [0018], lines 1-4).

Claim 25 is directed to a method for delivery of an agent to a delivery site in a subject, the method comprising the steps of: (a) implanting at the delivery site at least a distal portion of a device (page 4, paragraph [0013], lines 1-3), the device comprising: an elongate body comprising a proximal end defining an inlet, and a distal end defining an outlet, the elongate body defining a lumen in the elongate body, said lumen extending between the proximal and distal ends (page 14, paragraph [0063], lines 1-6); and a diffuser element operatively associated with the elongate body so as to define a diffusion space, wherein the elongate body distal end outlet is disposed in and in fluid communication with the diffusion space (page 20, paragraph [0083], lines 1-5), wherein the diffuser element is drug-permeable and

water-permeable (page 22, paragraph [0090], lines 1-5) so as to provide for dilution of a drug in the diffusion space and movement of drug out of the device (page 20, paragraph [0083], lines 5-7); and (b) introducing into the elongate body inlet a drug at a first concentration, wherein said drug moves through the elongate body lumen, out the elongate body outlet, and into the diffusion space, and further wherein water from the environment outside the device passes into the diffusion space through the diffuser element to dilute drug in the diffusion space to a second concentration, and wherein said diluted drug diffuses out through the diffuser element to exit the device at the delivery site in the subject (page 4, paragraph [0013], lines 3-8).

Claim 29 is directed to the device of claim 1 wherein the diffuser element comprises a polymeric film (page 37, paragraph [0136], lines 1-2).

Claim 30 is directed to the device of claim 29 wherein the diffuser element has a Diffusion Coefficient (DC) value in the range between 4.1×10^{-6} and 3.3×10^{-5} µg/cm/sec (page 38, paragraph [0137], lines 1-3).

Claim 31 is directed to the device of claim 1, wherein the elongate body is drug-impermeable wherein the diffuser element is substantially impermeable to drug and selectively permeable to water (page 2, paragraph [0007], lines 9-11).

Claim 32 is directed to the method of claim 25, wherein the elongate body lumen is at least partially filled with a drug formulation prior to said implanting (page 32, paragraph [0122], lines 6-8).

Claim 33 is directed to the device of claim 1, wherein the diffuser element is substantially impermeable to biological fluids or components of biological fluids (page 22, paragraph [0090], lines 1-3).

GROUNDS OF REJECTION TO BE REVIEWED ON APPEAL

Whether Claims 1, 2, 4, 6-13, 19-20, 22, 24, 25, 29 and 31-33 are unpatentable under 35 U.S.C. § 102(b) over Wolinsky et al. (USPN 5,087,244) .

Whether Claim 30 is unpatentable under 35 U.S.C. § 103(a) over Wolinsky et al. (the '244 patent).

Whether Claim 21 is unpatentable under 35 U.S.C. § 103(a) over Wolinsky et al. (the '244 patent) in view of Aoki et al. (USPN 6,113,915).

ARGUMENTS

I. Whether Claims 1, 2, 4, 6-13, 19-20, 22, 24, 25, 29 and 31-33 are unpatentable under 35 U.S.C. § 102(b) over Wolinsky et al. (the '244 patent).

This rejection as it is applied to each of the claims is addressed below.

A. Claim 1 is not anticipated by Wolinsky et al. (the '244 patent).

Claim 1 stands rejected under 35 U.S.C. § 102(b) as allegedly being anticipated by Wolinsky et al. Applicants respectfully disagree and traverse the rejection for the following reasons.

Anticipation under 35 U.S.C. §102 requires that a single prior art reference disclose every essential element of the claimed invention.[1] Exclusion of one claim element from a prior art reference is enough to negate anticipation by that reference.[2]

While anticipation requires that each claim element must be found in the cited reference, disclosure of the claim elements can be explicit or inherent.[3] In general, a limitation of the entire invention is inherent and in the public domain if it is the "natural result flowing from" the explicit disclosure of the prior art.[4] For example,

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[1] *Hybritech Inc. v. Monoclonal Antibodies, Inc.*, 802 F.2d 1367, 231 U.S.P.Q. (BNA) 81, 90 (Fed. Cir. 1986).
[2] *Atlas Powder Co. v. E.I. Du Pont de Nemours & Co.*, 750 F.2d 1569, 1574 224 U.S.P.Q. (BNA) 409, 411 (Fed. Cir. 1984).
[3] *In re Schreiber*, 128 F.3d 1473, 1477 (Fed. Cir. 1997); *Tyler Refrigeration v. Kysor Industrial Corp.*, 777 F.2d 687, 698, 227 U.S.P.Q. (BNA) 845, 846-47 (Fed. Cir. 1985).
[4] *See Eli Lilly & Co. v. Barr Labs., Inc.*, 251 F.3d 955, 970 (Fed. Cir. 2001); *see also, In re Kratz,* 592

where the prior art disclosed an antihistamine drug, but no express description of its metabolites, the prior art compound nevertheless inherently anticipated a broad claim to the metabolite compound when the metabolite was "necessarily and inevitably" produced by patients' bodies upon administering the drug.[5]

However, whether the prior art is relied upon for an explicit or inherent disclosure, the specific prior art embodiment relied upon must "itself [be] sufficiently described and enabled" in order to anticipate. For example, the court in *In re Seaborg*[6] found no inherent anticipation where the prior art process would have produced at most one billionth of a gram of the claimed isotope in forty tons of radioactive material, i.e., the isotope would have been undetectable.[7] Thus even in the context of anticipation by inherency, the basic patent law principle remains unchanged: "that which would literally infringe if later in time anticipates if earlier".[8] The prior art disclosure – whether explicit or inherent – must necessarily place the claimed invention in the hands of the public.

Finally, as set out in MPEP §2112, relying on an implicit (rather than explicit) disclosure in the prior art for the basis of a rejection must be supported by sound technical reasoning. As stated by the Board in *Ex parte Levy*,

> In relying upon the theory of inherency, the examiner must provide a basis in fact and/or technical reasoning to reasonably support the determination that the allegedly inherent characteristic necessarily flows from the teachings of the applied prior art.[9]

F.2d 1169, 1174 (CCPA 1979) (suggesting inherent anticipation of a compound even though the compound's existence was not known).

[5] *Schering Corp. v. Geneva Pharmaceuticals Inc.*, 339 F.3d 1373, 1377, 67 U.S.P.Q.2d (BNA) 1664, 1666 (Fed. Cir. 2003). *See also Toro Co. v. Deere & Co.*, 355 F.3d 1313 (Fed. Cir. 2004).

[6] *In re Seaborg*, 328 F.2d 996 (CCPA 1964).

[7] We note that the Federal Circuit cited *In re Seaborg* with approval in *Schering Corp. v. Geneva Pharm., Inc.*, 339 F.3d 1373, 1379 (Fed. Cir. 2003)(("[T]he claimed product, if it was produced in the Fermi process, was produced in such minuscule amounts and under such conditions that its presence was undetectable."). In this case, DCL [the claimed metabolite] forms in readily detectable amounts as shown by the extensive record evidence of testing done on humans to verify the formation of DCL upon ingestion of loratadine [the prior art compound].") *See also SmithKline Beecham Corp. v. Apotex Corp.*, 403 F.3d 1331 (Fed. Cir. 2005).

[8] *Bristol- Myers Squibb Co. v. Ben Venue Labs., Inc.*, 246 F.3d 1368, 1378 (Fed. Cir. 2001).

[9] *Ex parte Levy*, 17 USPQ2d 1461, 1464 (Bd. Pat. App. & Inter. 1990) (emphasis in original)

Claim 1 is directed to a device comprising an elongate body and a diffuser element which defines a diffusion space and is operatively associated with the elongate body. The elongate body comprises a lumen that extends from a proximal end inlet of the elongate body to a distal end outlet of the elongate body. The distal end outlet is disposed in and in fluid communication with the diffuser element which is drug-permeable and water-permeable and provides for dilution of a drug in the diffusion space. When in use, a drug flows through the elongate body lumen, out the delivery outlet, into the diffusion space, and out the diffuser element through diffuse delivery of the drug over an extended surface area.[10]

The claim term "diffuser element" is defined in the specification as the structure:

> responsible for *controlling* the egress of a drug, drug formulation or agent to a delivery site and/or the concentration or activity of the formulation following exit from the elongate body *prior to introduction to the delivery site*. The diffuser element comprises at least a diffusion barrier and a diffusion space (i.e., that area between the diffusion barrier and the elongate body), through which drug is *diffused*[11] (emphasis added).

The court has held that claim language describing a function can impart a structural limitation.[12] The specification repeatedly describes the "diffuser element" as having particular structural properties that confer its function in the device. For example, the specification teaches that the diffuser element comprises a diffusion barrier which "may be composed of a material that allows diffusion" or "may also be of a composition that allows an alteration of the activity of the drug as it passes through the diffusion barrier".[13] Further, the specification teaches that:

> Diffuser element body materials can vary according to a variety of factors such as the *desired permeability* (*e.g.*, selectively permeable to

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[10] Specification, pages 20-21, paragraphs [0083] and [0085].
[11] Specification, page 10, paragraph [0047].
[12] *In re Venezia*, 530 F.2d 956, 1976 CCPA LEXIS 186, 189 U.S.P.Q. (BNA) 149, 152 (C.C.P.A. 1976) (holding that the language "each sleeve of said pair *adapted to be fitted* over the insulating jacket" imparts a structural limitation to the sleeve; emphasis in original). Followed by *ISCO Intl., Inc. v. Conductus, Inc.*, 2003 U.S. Dist. LEXIS 1880. Cited by the Federal Circuit in *Pac-Tel, Inc. v. Amerace Corporation*, 903 F.2d 796, 1990 U.S. App. LEXIS 7475, 14 U.S.P.Q.2d (BNA) 1871 (Fed. Cir. 1990).
[13] Specification, page 10, paragraph [0046].

> an agent), ... For the example, the diffuser element can be microporous, a dense material, or an ion-exchange membrane.[14] (emphasis added).

Also, Claim 1 recites "the diffuser element is drug-permeable and water-permeable and provides for dilution of a drug in the diffusion space". The specification teaches that:

> Generally, the diffuser element is permeable or semi-permeable to the agent, and may also be permeable or impermeable to biological fluids from the external environment, such that the diffuser element permits egress of agent from the device assembly and to the delivery site ... .[15]

As such, the function of the diffuser element must have a structure comprising a permeable material that permits diffusion through it.

The Examiner asserts that Wolinsky et al. discloses "a balloon catheter having a flexible, inelastic cylindrical balloon at its distal end, the balloon having a plurality of regularly spaced minute openings through which medication may weep at a controlled, low flow rate".[16] When in use, the medication is introduced from a syringe or other pressure infusion device through an inflation lumen extending through the shaft of the catheter into the balloon, and then through the minute openings into the patient.[17] As set out in detail below, the balloon of Wolinsky et al. is not "a diffuser element" because **1) it does not provide for diffusion of a drug from the inside the balloon to the outside, 2) it does not provide for dilution of drug in a diffusion space of the device, and 3) it does not provide for a diffusion element that comprises a material that permits diffusion through it.** Therefore, Wollinsky does not disclose each and every element of the claimed invention.

1. The balloon of Wolinsky et al. is not "a diffuser element" because it does not provide for diffusion of a drug from the inside the balloon to the outside

[14] *Id.*, page 23, paragraph [0092].
[15] *Id.*, page 22, paragraph [0090].
[16] Wolinsky et al., col. 2, lines 7-11.
[17] *Id.* at col. 2, lines 11-32.

The Examiner alleges that "Wolinsky discloses . . . a diffuser element (16)".[18] However, the Examiner has not provided any evidence or reasoning to support this assertion.

Diffusion is a scientific term that refers to the random movement of free molecules or ions or small particles in solution or suspension under the influence of Brownian (thermal) motion toward a uniform distribution throughout the available volume. The thermal motion that influences diffusion is understood by the skilled person in the art to be a passive force, not an active force. Movement of agent from Applicants' device by diffusion would thus be recognized to be a passive process. In other words, a primary driving force for movement of drug out of the diffuser element and to the delivery site is the random (passive) movement of the agent molecules as a result of a concentration gradient established between a higher concentration of drug inside the diffuser element compared to a concentration of drug the outside the device at the delivery site in the body tissue.

The structural characteristics of the balloon of Wolinsky et al. are entirely different. Wolinsky et al. discloses that the device delivers drug from the balloon upon **application of 2-5 atm of pressure** to **force** the drug out of the openings of the balloon. Wolinsky et al. states that this provides a maximum flow rate of about 2 to 12 cc per minute, which is referred to as "weeping in nature".[19] Wolinsky et al. have no disclosure that drug delivery without the application of any force or pressure. Thus, the balloon structure of Wolinsky et al. does not provide for passive movement of drug by diffusion from inside the balloon to the outside. Instead, the drug is actively forced by application of pressure.

Further, Wolinsky disclose that when the liquid pressure is removed and the balloon is deflated, "[t]he balloon catheter then is withdrawn from the patient."[20] There is no diffusion of drug from the inside of the balloon to the outside as the balloon is removed from the patient's body when it is deflated.

[18] Office Action dated May 31, 2005, page 2.
[19] Wolinsky et al., col. 4, lines 19-36.
[20] *Id.*, col. 5, lines 45-49.

As such, the Examiner has not shown that the balloon of Wolinsky et al. is "a diffuser element" because the balloon of Wolinsky et al. does not does not allow diffusion of a drug from inside the balloon to the outside.

2. The balloon of Wolinsky et al. is not "a diffuser element [that provides] for dilution of a drug in the diffusion space" because it does not dilute the drug prior to egressing the device.

The Examiner points to no disclosure in Wolinsky regarding dilution of drug within the device, as required by the term "diffuser element" as defined. Rather than point to any such explicit disclosure, the Examiner states in a parenthetical:

> (The device is capable of providing for dilution of a drug. For example, when fluid pressure from the source of medicine is discontinued, some fluid from the patient's body may enter element 16. Or when the balloon is deflated by aspirating through the inflation/deflation lumen to cause the balloon to collapse, some fluid from the patient's body may enter element 16.)[21]

Applicants respectfully assert that Wolinsky et al. does not disclose a device that has "a diffuser element [that provides] for dilution of a drug in the diffusion space", because the balloon of Wolinsky et al. does not dilute the drug prior to egressing the device.

The Examiner has stated that the device of Wolinsky et al. is capable for dilution of a drug as "when fluid pressure from the source of medicine is discontinued, some fluid from the patient's body may enter element 16 [i.e., the balloon]", or "when the balloon is deflated by aspirating through the inflation/deflation lumen to cause the balloon to collapse, some fluid from the patient's body may enter element 16" (emphasis added).[22] From this the Examiner implies that the Wolinsky device inherently discloses dilution, However, the Federal Court has also held that certain result or characteristic may occur or be present in the prior art is not sufficient to establish the inherency of that result or characteristic.[23] The Examiner has not provided a basis in fact or technical reasoning to reasonably support that the

[21] Office Action dated January 24, 2006, page 2.
[22] Office Action dated May 31, 2005, pages 2-3.

assertion that when the balloon is deflated, body fluid would necessarily enter the balloon. Further, even assuming that body fluid enters the balloon when it is deflated, that such a result or characteristic may occur is insufficient to establish inherency.

As such, the Examiner has not shown that the balloon of Wolinsky et al. is "a diffuser element [that provides] for dilution of a drug in the diffusion space" because the balloon of Wolinsky et al. does not dilute the drug prior to egressing the device.

3. The balloon of Wolinsky et al. is not "a diffuser element" because it does not provide for a diffusion element that comprises a material that permits diffusion through it

As described earlier, the function of the diffuser element indicates that it has a structure made of a permeable material. In contrast, Wolinsky et al. describes their balloon catheter as "formed from various polymeric materials and desirably has a thin, flexible, preferably inelastic wall [and that a] preferred material is polyethylene terephthalate".[24] In clear distinction with the diffuser element of the claimed invention, the polyethylene terephthalate balloon catheter of Wolinsky et al. consists of a material that does not permit diffusion to take place through it. As explained above, the addition of the 25 micron holes do not render the Wolinsky balloon capable of diffusion because the material of the Wolinsky balloon is not permeable. As such, the structure of the Wolinsky balloon is entirely distinct from the claimed invention.

Thus, the Examiner has not shown that the balloon of Wolinsky et al. has a "a diffuser element" because the balloon of Wolinsky et al. does not have the structure of the diffusion element as taught in the specification.

In view of the foregoing reasons, the Applicants submit that Wolinsky et al. fails to disclose each and every element of the rejected Claim 1 and, therefore, do not anticipate Claim 1. As such, Applicants request that the Board overturn this rejection.

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[23] *In re Rijckaert*, 9 F.3d 1531, 1534, 28 USPQ2d 1955, 1957 (Fed. Cir. 1993).
[24] Wolinsky et al, col. 3, lines 47-50.

B. Claims 2, 8 and 10 are not anticipated by Wolinsky et al. (the '244 patent).

Claim 2, 8 and 10 stand rejected under 35 U.S.C. § 102(b) as allegedly being anticipated by Wolinsky et al. Applicants respectfully disagree and traverse the rejection for the following reasons.

The legal standard for anticipation under 35 U.S.C. § 102(b) and for finding anticipation based on inherency is provided above.

Claim 2 is directed to a device of Claim 1 wherein the diffuser element comprises a semipermeable membrane, a microporous membrane or an ion exchange membrane. Claim 8 is directed to a device of Claim 1 wherein the diffuser element is microporous. Claim 10 is directed to a device of Claim 1 wherein the diffuser element is an ion exchange membrane.

For the reasons set forth earlier, Wolinsky et al. does not anticipate the device of Claims 2, 8 and 10 because Wolinsky et al. teaches neither the elements of "a diffuser element" nor "a diffuser element [that provides] for dilution of a drug in the diffusion space".

Further, in regards to Claim 2, Wolinsky et al. does not teach that its balloon has "a semipermeable membrane".

The Examiner alleges that "the element 16 [i.e., the balloon] has minute holes (29) that is considered semipermeable since it allows through medication or fluid but not substances that are larger than the size of the holes."[25] The only teaching that Wolinsky et al. provides regarding the size of the holes is the following: "we have found that . . . holes, each about 25 microns in diameter has been satisfactory."[26] Wolinsky et al. provides no teaching about having holes smaller than 25 microns.

Applicants respectfully disagree with the Examiner's reasoning that a hole is semipermeable merely because it does not allow substances larger than its size to pass through. Under this reasoning, any hole of any size is semipermeable since one could always find a larger object that cannot pass through it. For example, a

[25] Office Action dated January 24, 2006, pages 2-3.
[26] Wolinsky et al., col. 4, lines 3-5.

mouse hole is semipermeable because a cat cannot pass through it, a cat door is semipermeable because a dog can not pass through it, etc. In other words, the *context* gives different meaning to the term semipermeable.

In the context of the disclosure of Wolinsky et al., a material having holes 25 microns in diameter is not semipermeable. The inflatable catheter of Wolinsky et al. is used in the blood vessel. It is well known in the art that in blood all the relevant particles are less than 25 microns in size, for example, red blood cells are 7-8 microns in diameter, and the largest white blood cells are monocytes which can reach 20 microns in diameter.[27] The size of the holes is not sufficient to exclude any relevant material in blood from passing through it. Thus the 25 micron holes do not render the balloon of Wolinsky et al. semipermeable in the context of its use. Accordingly, Wolinsky et al. fails to teach the semipermeable aspect of claim 2, contrary to the Examiner's position.

In contrast, the specification teaches that "the diffuser element is ... semi-permeable to the agent, and may also be ... semipermeable from the external environment, such that the diffuser element permits egress of agents from the device assembly ... while inhibiting or substantially inhibiting ingress of agents contained in the biological fluids into the diffuser element".[28] Wolinsky et al. does not teach or suggest a diffuser element (which must be semipermeable), and in particular fails to teach or suggest comprise "a semipermeable membrane, a microporous membrane or an ion exchange membrane".

Further, in regards to Claims 2 and 8, Wolinsky et al. does not teach that its balloon is "a microporous membrane".

The Examiner alleges that "the diffuser element [here the Examiner is referring to the balloon of the Wolinsky et al.] is microporous".[29] Mere 25 micron holes do not transform a balloon into a microporous membrane. As discussed above, a material having holes 25 microns in diameter is not considered

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[27] For example, red blood cells are 7-8 microns in diameter, and the largest white blood cells are monocytes which can reach 20 microns in diameter (Biology, Seventh Edition. Claude A. Villee. W.B. Saunders Co., Philadelphia, Pennsylvania (1977)).
[28] Specification, page 22, paragraph [0090].
[29] Office Action dated January 24, 2006, page 3.

microporous in the context of the claimed invention. As such, the balloon of Wolinsky et al. does not comprise "a microporous membrane".

Further, in regards to Claims 2 and 10, Wolinsky et al. does not teach that its balloon is "an ion exchange membrane".

The Examiner alleges that "the diffuser element [here the Examiner is referring to the balloon of the Wolinsky et al.] is an ion-exchange membrane, (citation omitted) since the holes (29) are capable of allowing an exchange of ions."[30] Just as it does not render the balloon catheter semipermeable, having 25 micron holes also does not transform a balloon into an ion-exchange membrane. It is well known in the art that an "ion-exchange membrane" is a thin material used for separating ions by allowing the preferential exchange of either cations or anions.[31] The 25 micron holes of the device of Wolinsky et al. are incapable of separating ions by allowing preferential exchange either cations or anions since they are too large to block passage of any ions. As such, the balloon of Wolinsky et al. is not "an ion exchange membrane"

In view of the foregoing reasons, the Applicants submit that Wolinsky et al. fails to disclose each and every element of the rejected Claims 2, 8 and 10. Accordingly, Wolinsky et al. does not anticipate Claims 2, 8 and 10. As such, Applicants request that the Board overturn these rejections.

C. Claim 4 is not anticipated by Wolinsky et al. (the '244 patent).

Claim 4 stands rejected under 35 U.S.C. § 102(b) as allegedly being anticipated by Wolinsky et al. Applicants respectfully disagree and traverse the rejection for the following reasons.

The legal standard for anticipation under 35 U.S.C. § 102(b) and for finding anticipation based on inherency is provided above.

Claim 4 is directed to a device of Claim 1 wherein the distal outlet of the elongate body is defined by an exit orifice of a drug delivery and the diffuser element is a cap in which the exit orifice is disposed.

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[30] *Id.*
[31] IUPAC Compendium of Chemical Terminology, 2d Edition (1997).

For the reasons set forth earlier, Wolinsky et al. does not anticipate the device of Claim 4 because Wolinsky et al. teaches neither the elements of "a diffuser element" nor "a diffuser element [that provides] for dilution of a drug in the diffusion space".

Further, Wolinsky et al. does not teach a cap in which the exit orifice is disposed. The Examiner alleges that "the diffuser element (16) is considered a cap in which the exit orifice is disposed"[32]. However, Figure 2 of Wolinsky, et al. shows the opening 20 leading into element 16 but not element 16 as a cap to opening 20:

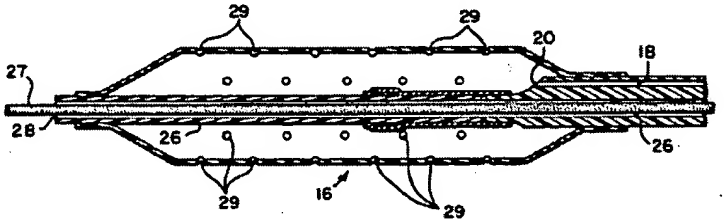
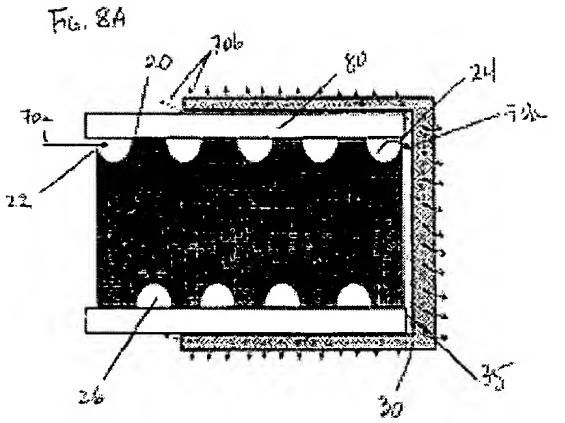
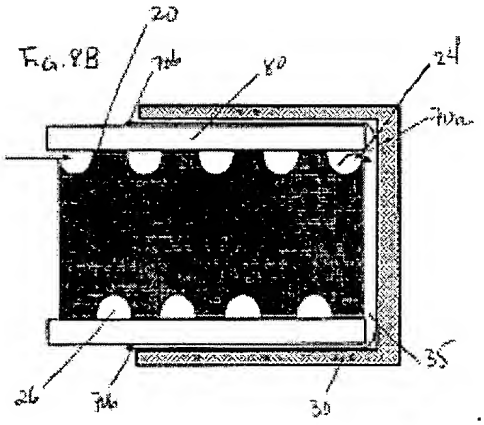


Fig. 2

In contrast, Figure 8 (panels A and B) of the specification provides an example of a diffuser element 30 that is a cap that is disposed over the distal end of the elongate body 20:

[32] Office Action dated January 24, 2006, page 3.





The device disclosed by Wolinsky et al. is structurally distinct from the diffuser element of Claim 4 which is a cap. Wolinsky et al. does not teach a diffuser element that is a cap.

In view of the foregoing reasons, the Applicants submit that Wolinsky et al. fails to disclose each and every element of the rejected Claim 4 and, therefore, cannot anticipate Claim 4. As such, Applicants request that the Board overturn this rejection.

D. Claim 6 is not anticipated by Wolinsky et al. (the '244 patent).

Claim 6 stands rejected under 35 U.S.C. § 102(b) as allegedly being anticipated by Wolinsky et al. Applicants respectfully disagree and traverse the rejection for the following reasons.

The legal standard for anticipation under 35 U.S.C. § 102(b) and for finding anticipation based on inherency is provided above.

Claim 6 is directed to a device of Claim 1 wherein the diffusion space is defined by an outer wall of the elongate body and an inner wall of the diffuser element.

For the reasons set forth earlier, Wolinsky et al. does not anticipate the device of Claim 6 because Wolinsky et al. teaches neither the elements of "a diffuser element" nor "a diffuser element [that provides] for dilution of a drug in the diffusion space".

In view of the foregoing reasons, the Applicants submit that Wolinsky et al. fails to disclose each and every element of the rejected Claim 6 and, therefore, do not anticipate Claim 6. As such, Applicants request that the Board overturn this rejection.

E. Claim 7 is not anticipated by Wolinsky et al. (the '244 patent).

Claim 7 stands rejected under 35 U.S.C. § 102(b) as allegedly being anticipated by Wolinsky et al. Applicants respectfully disagree and traverse the rejection for the following reasons.

The legal standard for anticipation under 35 U.S.C. § 102(b) and for finding anticipation based on inherency is provided above.

Claim 7 is directed to a device of Claim 1 wherein the diffuser element surrounds at least a portion of said elongate body.

For the reasons set forth earlier, Wolinsky et al. does not anticipate the device of Claim 7 because Wolinsky et al. teaches neither the elements of "a diffuser element" nor "a diffuser element [that provides] for dilution of a drug in the diffusion space".

In view of the foregoing reasons, the Applicants submit that Wolinsky et al. fails to disclose each and every element of the rejected Claim 7 and, therefore, do not anticipate Claim 7. As such, Applicants request that the Board overturn this rejection.

F. Claim 9 is not anticipated by Wolinsky et al. (the '244 patent).

Claim 9 stands rejected under 35 U.S.C. § 102(b) as allegedly being anticipated by Wolinsky et al. Applicants respectfully disagree and traverse the rejection for the following reasons.

The legal standard for anticipation under 35 U.S.C. § 102(b) and for finding anticipation based on inherency is provided above.

Claim 9 is directed to a device of Claim 1 wherein the diffuser element is a dense membrane.

For the reasons set forth earlier, Wolinsky et al. does not anticipate the device of Claim 9 because Wolinsky et al. teaches neither the elements of "a diffuser element" nor "a diffuser element [that provides] for dilution of a drug in the diffusion space".

Further, for the reasons stated earlier, the Wolinsky et al. discloses a balloon catheter made of polyethylene terephthalate. Polyethylene terephthalate is not a permeable material and thus can not serve as a dense membrane having the properties required by the claim.

In view of the foregoing reasons, the Applicants submit that Wolinsky et al. fails to disclose each and every element of the rejected Claim 9 and, therefore, do not anticipate Claim 9. As such, Applicants request that the Board overturn this rejection.

G. Claim 11 is not anticipated by Wolinsky et al. (the '244 patent).

Claim 11 stands rejected under 35 U.S.C. § 102(b) as allegedly being anticipated by Wolinsky et al. Applicants respectfully disagree and traverse the rejection for the following reasons.

The legal standard for anticipation under 35 U.S.C. § 102(b) and for finding anticipation based on inherency is provided above.

Claim 11 is directed to a device of Claim 1 wherein the diffuser element distal end extends distally beyond the elongate body distal end.

For the reasons set forth earlier, Wolinsky et al. does not anticipate the device of Claim 11 because Wolinsky et al. teaches neither the elements of "a diffuser element" nor "a diffuser element [that provides] for dilution of a drug in the diffusion space".

In view of the foregoing reasons, the Applicants submit that Wolinsky et al. fails to disclose each and every element of the rejected Claim 11 and, therefore, do not anticipate Claim 11. As such, Applicants request that the Board overturn this rejection.

H. Claim 12 is not anticipated by Wolinsky et al. (the '244 patent).

Claim 12 stands rejected under 35 U.S.C. § 102(b) as allegedly being anticipated by Wolinsky et al. Applicants respectfully disagree and traverse the rejection for the following reasons.

The legal standard for anticipation under 35 U.S.C. § 102(b) and for finding anticipation based on inherency is provided above.

Claim 12 is directed to a device of Claim 1 and has the further element that the diffuser element is a ring-shaped element.

For the reasons set forth earlier, Wolinsky et al. does not anticipate the device of Claim 12 because Wolinsky et al. teaches neither the elements of "a diffuser element" nor "a diffuser element [that provides] for dilution of a drug in the diffusion space".

Further, Wolinsky et al. does not teach that its balloon is "a ring-shaped element".

The Examiner alleges that "the diffuser element [here the Examiner is referring to the balloon of the Wolinsky et al.] distal [*sic*] is a ring-shaped element, see Figure 2."[33] However Wolinsky et al. discloses that the balloon is "cylindrical"[34] and Figure 2, to which the Examiner refers, depicts the cross-section of a cylindrical shaped balloon:

[33] Office Action dated January 24, 2006, page 3.
[34] Wolinsky et al., col. 2, line 8.

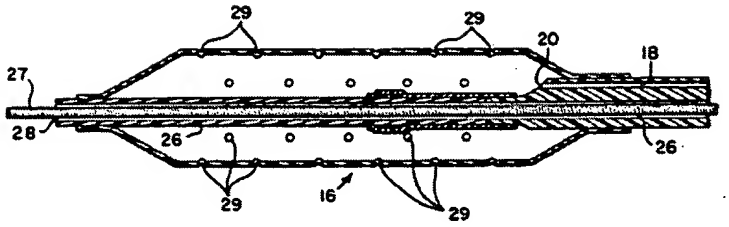
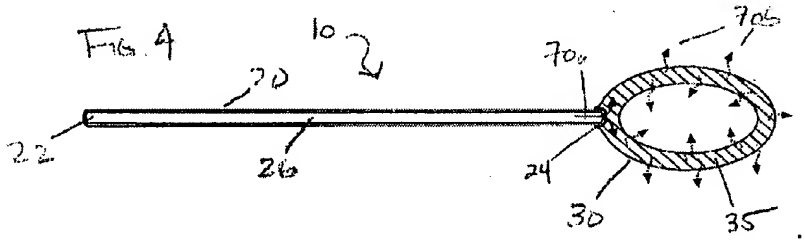


Fig. 2

In contrast, Figure 4 of the specification provides an example of a "ring-shaped element":



As such, it is clear the device disclosed by Wolinsky et al. is starkly distinct from the ring-shaped diffuser element of Claim 12. Wolinsky et al. does not teach a diffuser element that is a ring-shaped element.

In view of the foregoing reasons, the Applicants submit that Wolinsky et al. fails to disclose each and every element of the rejected Claim 12 and, therefore, do not anticipate Claim 12. As such, Applicants request that the Board overturn this rejection.

I. Claim 13 is not anticipated by Wolinsky et al. (the '244 patent).

Claim 13 stands rejected under 35 U.S.C. § 102(b) as allegedly being anticipated by Wolinsky et al. Applicants respectfully disagree and traverse the rejection for the following reasons.

The legal standard for anticipation under 35 U.S.C. § 102(b) and for finding anticipation based on inherency is provided above.

Claim 13 is directed to a device of Claim 1 wherein the diffuser element is selectively permeable to water.

For the reasons set forth earlier, Wolinsky et al. does not anticipate the device of Claim 14 because Wolinsky et al. teaches neither the elements of "a diffuser element" nor "a diffuser element [that provides] for dilution of a drug in the diffusion space".

Further, Wolinsky et al. does not teach that its balloon is "selectively permeable to water".

It is well-settled that functional claim language can impart a structural limitation to an element.35 In order for a diffuser element to have the function of being "selectively permeable to water", the element must have a structure or composition that has that imparts this particular property.

The Examiner alleges that "the diffuser element [here the Examiner is referring to the balloon of the Wolinsky et al.] is selectively permeable to water"[36] and merely cites to the section in Wolinsky et al. disclosing the holes that are 25 microns in diameter.[37] The 25 micron holes of the device of Wolinsky et al. are not selectively permeable to water. Such holes would permit any molecule, ion, or particle less than 25 microns to pass through. As explained earlier, such holes would even allow red and white blood cells to pass through.

In view of the foregoing reasons, the Applicants submit that Wolinsky et al. fails to disclose each and every element of the rejected Claim 13 and, therefore, do not anticipate Claim 13. As such, Applicants request that the Board overturn this rejection.

J. Claim 19 is not anticipated by Wolinsky et al. (the '244 patent).

Claim 19 stands rejected under 35 U.S.C. § 102(b) as allegedly being anticipated by Wolinsky et al. Applicants respectfully disagree and traverse the rejection for the following reasons.

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[35] *In re Venezia*, 530 F.2d 956, 1976 CCPA LEXIS 186, 189 U.S.P.Q. (BNA) 149, 152 (C.C.P.A. 1976) (holding that the language "each sleeve of said pair *adapted to be fitted* over the insulating jacket" imparts a structural limitation to the sleeve; emphasis in original). Followed by *ISCO Intl., Inc. v. Conductus, Inc.*, 2003 U.S. Dist. LEXIS 1880. Cited by the Federal Circuit in *Pac-Tel, Inc. v. Amerace Corporation*, 903 F.2d 796, 1990 U.S. App. LEXIS 7475, 14 U.S.P.Q.2d (BNA) 1871 (Fed. Cir. 1990).
[36] Office Action dated January 24, 2006, page 3.
[37] Wolinsky et al., col. 4, lines 3-5.

The legal standard for anticipation under 35 U.S.C. § 102(b) and for finding anticipation based on inherency is provided above.

Claim 19 is directed to a device of Claim 1 wherein the elongate body lumen is adapted for delivery of agent at a low volume rate.

For the reasons set forth earlier, Wolinsky et al. does not anticipate the device of Claim 19 because Wolinsky et al. teaches neither the elements of "a diffuser element" nor "a diffuser element [that provides] for dilution of a drug in the diffusion space".

Further, Wolinsky et al. does not teach that its balloon catheter has an "elongate body lumen adapted for delivery for delivery of agent at a low volume rate".

Claim language describing a function can impart a structural limitation.[38] As such, the element to be "adapted for delivery of agent at a low volume rate" describes a function that imparts a structure. Indeed, Claim 19 recites the phrase "adapted for" which was found by the court in *In re Venezia* to particularly signal that the subsequent claim limitations can be construed to impart a structural limitation.[39]

In order for the device to be "adapted for delivery of agent at a low volume rate", it must have a structure that provides for this function. For example, the specification teaches that "in certain embodiments, the inner diameter is compatible for drug delivery at relatively low volume rates, e.g., as low as about 0.01 µl per day".[40] This means that in order for the claimed invention to have a function of "delivery of agent at a low volume rate", the structure of the elongate body lumen diameter of the device must be compatible for such a low volume rate, i.e. a small diameter. Wolinsky et al. discloses the balloon catheter provides a flow rate of "a few cubic centimeters per minute".[41] The difference in flow rate is more than 8

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[38] *In re Venezia*, 530 F.2d 956, 1976 CCPA LEXIS 186, 189 U.S.P.Q. (BNA) 149, 152 (C.C.P.A. 1976) (holding that the language "each sleeve of said pair *adapted to be fitted* over the insulating jacket" imparts a structural limitation to the sleeve; emphasis in original). Followed by *ISCO Intl., Inc. v. Conductus, Inc.*, 2003 U.S. Dist. LEXIS 1880. Cited by the Federal Circuit in *Pac-Tel, Inc. v. Amerace Corporation*, 903 F.2d 796, 1990 U.S. App. LEXIS 7475, 14 U.S.P.Q.2d (BNA) 1871 (Fed. Cir. 1990).
[39] *Id.* Specifically, the court in *In re Venezia* found that the language "each sleeve of said pair *adapted to be fitted* over the insulating jacket" (emphasis in original) imparted a structural limitation to the sleeve.
[40] Specification, page. 19, paragraph [0081].
[41] Wolinsky et al., col. 2, lines 18-19.

orders of magnitude. In other words, Wolinsky et al. does not teach any structure that would provide for the low volume rate delivery of the claimed invention.

In view of the foregoing reasons, the Applicants submit that Wolinsky et al. fails to disclose each and every element of the rejected Claim 19 and, therefore, do not anticipate Claim 19. As such, Applicants request that the Board overturn this rejection.

K. Claim 20 is not anticipated by Wolinsky et al. (the '244 patent).

Claim 20 stands rejected under 35 U.S.C. § 102(b) as allegedly being anticipated by Wolinsky et al. Applicants respectfully disagree and traverse the rejection for the following reasons.

The legal standard for anticipation under 35 U.S.C. § 102(b) and for finding anticipation based on inherency is provided above.

Claim 20 is directed to a drug delivery device comprising the device of Claim 1 operably attached to a drug reservoir.

For the reasons set forth earlier, Wolinsky et al. does not anticipate the device of Claim 20 because Wolinsky et al. teaches neither the elements of "a diffuser element" nor "a diffuser element [that provides] for dilution of a drug in the diffusion space".

In view of the foregoing reasons, the Applicants submit that Wolinsky et al. fails to disclose each and every element of the rejected Claim 20 and, therefore, do not anticipate Claim 20. As such, Applicants request that the Board overturn this rejection.

L. Claim 22 is not anticipated by Wolinsky et al. (the '244 patent).

Claim 22 stands rejected under 35 U.S.C. § 102(b) as allegedly being anticipated by Wolinsky et al. Applicants respectfully disagree and traverse the rejection for the following reasons.

The legal standard for anticipation under 35 U.S.C. § 102(b) and for finding anticipation based on inherency is provided above.

Claim 22 is directed to a drug delivery device comprising the device of Claim 20 wherein the drug is delivered in microliter or submicroliter quantities per day.

For the reasons set forth earlier, Wolinsky et al. does not anticipate the device of Claim 22 because Wolinsky et al. teaches neither the elements of "a diffuser element" nor "a diffuser element [that provides] for dilution of a drug in the diffusion space".

Further, Wolinsky et al. does not teach that its balloon catheter delivers drug in "microliter or submicroliter quantitities per day".

Claim language describing a function can impart a structural limitation.[42] In order for the device to deliver drug in "microliter or submicroliter quantities per day", it must have a structure that is compatible with this function. For example, the structure of the inner diameter must be very small; the specification teaches that "in certain embodiments, the inner diameter is compatible for drug delivery at relatively low volume rates, e.g., as low as about 0.01 µl per day".[43] As described above, Wolinsky et al. at best disclose, a cathether with such an inner diameter that allows a flow rate of "a few cubic centimeters per minute".[44] The difference in flow rate is more than 8 orders of magnitude. In other words, Wolinsky et al. does not teach the small elongate body lumen diameter of the claimed invention.

In view of the foregoing reasons, the Applicants submit that Wolinsky et al. fails to disclose each and every element of the rejected Claim 22 and, therefore, do not anticipate Claim 22. As such, Applicants request that the Board overturn this rejection.

M. Claim 24 is not anticipated by Wolinsky et al. (the '244 patent).

Claim 24 stands rejected under 35 U.S.C. § 102(b) as allegedly being anticipated by Wolinsky et al. Applicants respectfully disagree and traverse the rejection for the following reasons.

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[42] *In re Venezia*, 530 F.2d 956, 1976 CCPA LEXIS 186, 189 U.S.P.Q. (BNA) 149, 152 (C.C.P.A. 1976) (holding that the language "each sleeve of said pair *adapted to be fitted* over the insulating jacket" imparts a structural limitation to the sleeve; emphasis in original). Followed by *ISCO Intl., Inc. v. Conductus, Inc.*, 2003 U.S. Dist. LEXIS 1880. Cited by the Federal Circuit in *Pac-Tel, Inc. v. Amerace Corporation*, 903 F.2d 796, 1990 U.S. App. LEXIS 7475, 14 U.S.P.Q.2d (BNA) 1871 (Fed. Cir. 1990).

[43] Specification, page. 19, paragraph [0081].

The legal standard for anticipation under 35 U.S.C. § 102(b) and for finding anticipation based on inherency is provided above.

Claim 24 is directed to a method of Claim 25 wherein the formulation is introduced into the inlet at a low volume rate.

For the reasons set forth below, Wolinsky et al. does not anticipate the method of Claim 25 because Wolinsky et al. does not teach the device, as used in the method of Claim 25, which has the elements of "a diffuser element" nor "a diffuser element [that provides] for dilution of a drug in the diffusion space". Further, Wolinsky et al. does not teach a device which during use has "water from the environment outside the device pass[] into the diffusion space through the diffuser element to dilute drug in the diffusion space".

Further, Wolinsky et al. does not teach that the drug is introduced into its balloon catheter "at a low volume rate".

Wolinsky fails to teach or suggest a method requiring low volume rate delivery. "Low volume rate" is defined in the specification:

> The term "low volume rate delivery" as used herein is generally meant to refer to delivery of a liquid or semisolid drug at a volume rate of from about 0.01 μl per day to about 200 μl per day, usually about 0.04 μl per day to about 20 μl per day, more usually about 0.1 μl per day or about 1.0 μl per day.[45]

Wolinsky at best discloses delivery of a "flow rate of a few cubic centimeters per minute." This rate is far in excess of a "low volume rate" as defined in the specification. Moreover, it is unlikely that a low volume rate of delivery would provide for drug delivery as taught by Wolinsky, which requires the balloon be inflated and drug "forced" out the balloon.

In view of the foregoing reasons, the Applicants submit that Wolinsky et al. fails to disclose each and every element of the rejected Claim 24 and, therefore, do not anticipate Claim 24. As such, Applicants request that the Board overturn this rejection.

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[44] Wolinsky et al., col. 2, lines 18-19.

N. Claim 25 is not anticipated by Wolinsky et al. (the '244 patent).

Claim 25 stands rejected under 35 U.S.C. § 102(b) as allegedly being anticipated by Wolinsky et al. Applicants respectfully disagree and traverse the rejection for the following reasons.

The legal standard for anticipation under 35 U.S.C. § 102(b) and for finding anticipation based on inherency is provided above.

Claim 25 is directed to a method for delivery of an agent to a delivery site in a subject by (a) implanting at the delivery site a device comprising: an elongate body and a diffuser element operatively associated with the elongate body so as to define a diffusion space, which is drug-permeable and water-permeable so as to provide for dilution of a drug in the diffusion space and movement of drug out of the device; and (b) introducing into the elongate body a drug at a first concentration, wherein the drug moves through the elongate body and into the diffusion space, wherein water from the environment outside the device passes into the diffusion space through the diffuser element to dilute drug in the diffusion space to a second concentration, and wherein the diluted drug diffuses out through the diffuser element to exit the device.

For the reasons set forth earlier, Wolinsky et al. does not anticipate the method of Claim 25 because Wolinsky et al. does not teach a device with either "a diffuser element" or "a diffuser element [that provides] for dilution of a drug in the diffusion space". As a function of the diffuser element is that it must allow for diluted drug to diffuse out through the diffuser element to exit the device, this means the diffuser element must have a composition comprising a permeable material that permits diffusion through it.

Further, Wolinsky et al. does not teach a device which during use has "water from the environment outside the device pass[] into the diffusion space through the diffuser element to dilute drug in the diffusion space".

For the reasons provided earlier, the Wolinsky et al. does not teach a device, which during use, allows water from the outside to pass into a diffusion space to dilute drug. Since the device of Wolinsky et al. does not dilute drug then it cannot

[45] Specification, page 11, paragraph [0053].

carrying a step which results in drug being diluted. As such, the device of Wolinsky et al. does not carry out this step during use. Also, as described earlier, the Wolinsky et al. balloon catheter consists of a material, such as polyethylene terephthalate, that does not permit diffusion to take place through it. The addition of the 25 micron holes do not render the Wolinsky balloon capable of diffusion because the material of the Wolinsky balloon is not permeable. As such, the structure of the Wolinsky balloon is entirely distinct from the diffusion element of the claimed method.

In view of the foregoing reasons, the Applicants submit that Wolinsky et al. fails to disclose each and every element of the rejected Claim 25 and, therefore, do not anticipate Claim 25. As such, Applicants request that the Board overturn this rejection.

O. Claim 29 is not anticipated by Wolinsky et al. (the '244 patent).

Claim 29 stands rejected under 35 U.S.C. § 102(b) as allegedly being anticipated by Wolinsky et al. Applicants respectfully disagree and traverse the rejection for the following reasons.

The legal standard for anticipation under 35 U.S.C. § 102(b) and for finding anticipation based on inherency is provided above.

Claim 29 is directed to the device of Claim 1 wherein the diffuser element comprises a polymeric film.

For the reasons set forth earlier, Wolinsky et al. does not anticipate the device of Claim 29 because Wolinsky et al. teaches neither the elements of "a diffuser element" nor "a diffuser element [that provides] for dilution of a drug in the diffusion space".

In view of the foregoing reasons, the Applicants submit that Wolinsky et al. fails to disclose each and every element of the rejected Claim 29 and, therefore, do not anticipate Claim 29. As such, Applicants request that the Board overturn this rejection.

P. Claim 31 is not anticipated by Wolinsky et al. (the '244 patent).

Claim 31 stands rejected under 35 U.S.C. § 102(b) as allegedly being anticipated by Wolinsky et al. Applicants respectfully disagree and traverse the rejection for the following reasons.

The legal standard for anticipation under 35 U.S.C. § 102(b) and for finding anticipation based on inherency is provided above.

Claim 31 is directed to a device of Claim 1 wherein the elongate body is drug-impermeable wherein the diffuser element is substantially impermeable to drug and selectively permeable to water.

For the reasons set forth earlier, Wolinsky et al. does not anticipate the device of Claim 31 because Wolinsky et al. teaches neither the elements of "a diffuser element" nor "a diffuser element [that provides] for dilution of a drug in the diffusion space".

Further, Wolinsky et al. does not teach that its balloon is "selectively permeable to water".

Claim language describing a function can impart a structural limitation.[46] As such, the element "selectively permeable to water" is functional language that necessarily imparts a structure to the diffuser element.[47] In order for the diffuser element to have the function of being "selectively permeable to water", the diffuser element must have a structure or composition that has that imparts this particular property.

The Examiner alleges that "the diffuser element [here the Examiner is referring to the balloon of the Wolinsky et al.] is selectively permeable to water"[48] and merely cites to the section in Wolinsky et al. disclosing the holes that are 25

[46] *In re Venezia*, 530 F.2d 956, 1976 CCPA LEXIS 186, 189 U.S.P.Q. (BNA) 149, 152 (C.C.P.A. 1976) (holding that the language "each sleeve of said pair *adapted to be fitted* over the insulating jacket" imparts a structural limitation to the sleeve; emphasis in original). Followed by *ISCO Intl., Inc. v. Conductus, Inc.*, 2003 U.S. Dist. LEXIS 1880. Cited by the Federal Circuit in *Pac-Tel, Inc. v. Amerace Corporation*, 903 F.2d 796, 1990 U.S. App. LEXIS 7475, 14 U.S.P.Q.2d (BNA) 1871 (Fed. Cir. 1990).
[47] *In re Venezia*, 530 F.2d 956, 1976 CCPA LEXIS 186, 189 U.S.P.Q. (BNA) 149, 152 (C.C.P.A. 1976).
[48] Office Action dated January 24, 2006, page 3.

microns in diameter.[49] The 25 micron holes of the device of Wolinsky et al. are not selectively permeable to water. Such holes would permit any molecule, ion, or particle less than 25 microns to pass through. As explained earlier, such holes would even allow red and white blood cells to pass through. As such, the balloon of Wolinsky et al. must not be selectively permeable to water.

In view of the foregoing reasons, the Applicants submit that Wolinsky et al. fails to disclose each and every element of the rejected Claim 31 and, therefore, do not anticipate Claim 31. As such, Applicants request that the Board overturn this rejection.

Q. Claim 32 is not anticipated by Wolinsky et al. (the '244 patent).

Claim 32 stands rejected under 35 U.S.C. § 102(b) as allegedly being anticipated by Wolinsky et al. Applicants respectfully disagree and traverse the rejection for the following reasons.

The legal standard for anticipation under 35 U.S.C. § 102(b) and for finding anticipation based on inherency is provided above.

Claim 32 is directed to the method of Claim 25 wherein the elongate body lumen is at least partially filled with drug formulation prior to the implanting.

For the reasons set forth above, Wolinsky et al. does not anticipate the method of Claim 25 because Wolinsky et al. does not teach the device, as used in the method of Claim 25, which has the elements of "a diffuser element" nor "a diffuser element [that provides] for dilution of a drug in the diffusion space". Further, Wolinsky et al. does not teach a device which during use has "water from the environment outside the device pass[] into the diffusion space through the diffuser element to dilute drug in the diffusion space".

In view of the foregoing reasons, the Applicants submit that Wolinsky et al. fails to disclose each and every element of the rejected Claim 32 and, therefore, do not anticipate Claim 32. As such, Applicants request that the Board overturn this rejection.

[49] Wolinsky et al., col. 4, lines 3-5.

R. Claim 33 is not anticipated by Wolinsky et al. (the '244 patent).

Claim 33 stands rejected under 35 U.S.C. § 102(b) as allegedly being anticipated by Wolinsky et al. Applicants respectfully disagree and traverse the rejection for the following reasons.

The legal standard for anticipation under 35 U.S.C. § 102(b) and for finding anticipation based on inherency is provided above.

Claim 33 is directed to a device of Claim 1 wherein the diffuser element is substantially impermeable to biological fluids or components of biological fluids.

For the reasons set forth earlier, Wolinsky et al. does not anticipate the device of Claim 33 because Wolinsky et al. teaches neither the elements of "a diffuser element" nor "a diffuser element [that provides] for dilution of a drug in the diffusion space".

Further, Wolinsky et al. does not teach that its balloon is "substantially impermeable to biological fluids or components of biological fluids".

Claim language describing a function can impart a structural limitation.[50] The function of the diffuser element imparts a structure, i.e. the diffuser element comprises a semipermeable material, as discussed above. The Examiner alleges that "the diffuser element [here the Examiner is referring to the balloon of the Wolinsky et al.] is substantially impermeable to biological fluids or components of biological fluids (i.e., biological fluids or components of biological fluids that are larger than the size of the openings in the device)."[51] For the reasons set forth earlier, Wolinsky et al. only discloses that the balloon have holes of 25 microns in diameter, and such holes will permit any molecule, ion, or particle less than 25 microns to pass through, including very large particles such as red and white blood cells. Since it is hard to imagine that there are many (if any) relevant particles in blood that are larger than white blood cells, the balloon of Wolinsky et al. must not

[50] *In re Venezia*, 530 F.2d 956, 1976 CCPA LEXIS 186, 189 U.S.P.Q. (BNA) 149, 152 (C.C.P.A. 1976) (holding that the language "each sleeve of said pair *adapted to be fitted* over the insulating jacket" imparts a structural limitation to the sleeve; emphasis in original). Followed by *ISCO Intl., Inc. v. Conductus, Inc.*, 2003 U.S. Dist. LEXIS 1880. Cited by the Federal Circuit in *Pac-Tel, Inc. v. Amerace Corporation*, 903 F.2d 796, 1990 U.S. App. LEXIS 7475, 14 U.S.P.Q.2d (BNA) 1871 (Fed. Cir. 1990).
[51] Office Action dated January 24, 2006, page 4.

be substantially impermeable to such biological fluids or components of biological fluids.

In view of the foregoing reasons, the Applicants submit that Wolinsky et al. fails to disclose each and every element of the rejected Claim 33 and, therefore, do not anticipate Claim 33. As such, Applicants request that the Board overturn this rejection.

2. Whether Claim 30 is unpatentable under 35 U.S.C. § 103(a) over Wolinsky et al. (the '244 patent).

Claim 30 stands rejected under 35 U.S.C. § 103(a) as allegedly being rendered obvious by Wolinsky et al. Applicants respectfully disagree and traverse the rejection for the following reasons.

Under 35 U.S.C. §103(a) a claim of a patent is invalid for obviousness "if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which [the] subject matter pertains." Obviousness under §103 must be determined by considering: (1) the scope and content of the prior art, (2) the differences between the prior art and the patent claim, and (3) the level of ordinary skill in the pertinent art.[52] Based on the results of these inquiries, the court then determines whether the claimed invention as a whole would have been obvious to one of ordinary skill in the appropriate art at the time the invention was made.[53] In addition, in order to establish a *prima facie* case of obviousness, the references must be considered in their entirety for what they fairly teach to one of ordinary skill in the art.[54] Finally, a *prima facie* obviousness requires that all the claim limitations must be taught or suggested by the prior art.[55]

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[52] *Graham v. John Deere Co.*, 333 U.S. 1, 148 U.S.P.Q. 459 (1966).
[53] *Medtronic, Inc. v. Cardiac Pacemakers, Inc.*, 721 F.2d 1563, 1567 (Fed. Cir. 1983).
[54] *In re Hedges*, 228 U.S.P.Q. (BNA) 685 (Fed. Cir. 1986).
[55] *In re Royka*, 490 F.2d 981, 180 USPQ 580 (CCPA 1974).

The Federal Circuit has held that if a proposed modification would render the prior art invention being modified unsatisfactory for its intended purpose, then there is no suggestion or motivation to make the proposed modification.[56] In addition, if the proposed modification of the prior art would change the principle of operation of the prior art invention being modified, then *prima facie* obviousness is not sufficiently established.[57]

Claim 30 requires that the diffuser element have a Diffusion Coefficient (DC) value in the range between 4.1×10^{-6} and 3.3×10^{-5} µg/cm/sec.

For the reasons set forth earlier, Wolinsky et al. does not teach or suggest the elements of "a diffuser element" nor "a diffuser element [that provides] for dilution of a drug in the diffusion space". The Examiner alleges that "it would have been obvious to form the diffuser element [i.e., the Examiner means the balloon of Wolinsky et al.] in which the holes' size and spacing is selected such that it has the specific [DC] as claimed, since Wolinsky teaches that medications may have viscosity and flow characteristics that might require modifications to the holes."[58] However, the modifications that Wolinsky et al. are referring to are those to deliver medications to the patient using its forced pressure method. There is no suggestion or motivation to convert the balloon of Wolinsky et al. into a diffuser element or to use it to dilute the drug to be delivered.

The Examiner's proposal to modify the Wolinsky balloon to deliver drug with a Diffusion Coefficient (DC) value in the range between 4.1×10^{-6} and 3.3×10^{-5} µg/cm/sec would render the Wolinsky balloon unsatisfactory for its intended purpose. In order to deliver drug, Wolinsky et al. teaches application of 2-5 atm of pressure to force the drug out of the openings of the balloon so as to penetrate a vessel wall of the patient.[59] Modifying the structure of the Wolinsky balloon to obtain a DC value in the range between 4.1×10^{-6} and 3.3×10^{-5} µg/cm/sec would be contrary to the principle taught in Wolinsky to deliver drug by force (as opposed to

[56] *In re Gordon*, 733 F.2d 900, 221 USPQ 1125 (Fed. Cir. 1984).
[57] *In re Ratti*, 270 F.2d 810, 123 USPQ 349 (CCPA 1959).
[58] Office Action dated January 24, 2006, page 5.
[59] Wolinsky et al., col. 4, lines 19-36.

diffusion). Why would one adapt the Wolinsky balloon in such a manner when it may require even more force be applied to deliver drug?

Furthermore, attempting to practice the Wolinsky balloon by diffusion would mean radically changing the principle of operation of the Wolinsky balloon from an active application of pressure to passive diffusion. The principle of operation of the Wolinsky balloon catheter is the active application of 2-5 atm force to push the drug from the balloon catheter to penetrate the vessel wall of the patient. This is the opposite of the claimed invention.

In view of the foregoing reasons, the Applicants submit that Wolinsky et al. fails to teach or suggest each and every element of the rejected Claim 30 and, therefore, do not render obvious Claim 30. As such, Applicants request that the Board overturn this rejection.

3. Whether Claim 21 is unpatentable under 35 U.S.C. § 103(a) over Wolinsky et al. (the '244 patent) in view of Aoki et al. (the '915 patent).

Claim 21 stands rejected under 35 U.S.C. § 103(a) as allegedly being rendered obvious by Wolinsky et al. in view of Aoki et al. Applicants respectfully disagree and traverse the rejection for the following reasons.

The legal standard for obviousness under 35 U.S.C. § 103(a) is provided above.

Claim 21 is directed to the drug delivery system of Claim 20 (which in turn comprises the device of Claim 1) wherein the drug reservoir contains Baclofen.

For the reasons set forth earlier, Wolinsky et al. does not teach or suggest the elements of "a diffuser element" nor "a diffuser element [that provides] for dilution of a drug in the diffusion space".

Aoki et al. disclose treating spasticity in patient by intrathecal administration of Baclofen. As such, Aoki et al. do not cure the deficiency of the Wolinsky et al. disclosure as Aoki et al. also do not disclose or suggest these missing claim elements. The combination of Wolinsky et al. and Aoki et al. would at best led one skilled in the art to use the balloon catheter of Wolinsky et al. to deliver Baclofen to a

patient by applying a force of 2-5 atm of pressure to force Baclofen out of the openings of the balloon into the patient's blood vessel walls.

In view of the foregoing reasons, the Applicants submit that Wolinsky et al. and Aoki et al., either together or alone, fail to teach or suggest each and every element of the rejected Claim 21 and, therefore, do not render obvious Claim 21. As such, Applicants request that the Board overturn this rejection.

SUMMARY

Claims 1, 2, 4, 6-13, 19-20, 22, 24, 25, 29 and 31-33 are not anticipated by Wolinsky et al. as the elements "a diffuser element" and "a diffuser element [that provides] for dilution of a drug in the diffusion space", among other elements, are not taught by Wolinsky et al. Applicants request that the Board overturn this rejection.

Claim 30 is not rendered obvious by Wolinsky et al. as the elements "a diffuser element" and "a diffuser element [that provides] for dilution of a drug in the diffusion space" are not taught or suggested by Wolinsky et al. Applicants request that the Board overturn this rejection.

Claim 21 is not rendered obvious by Wolinsky et al. in view of Aoki et al. as the elements "a diffuser element" and "a diffuser element [that provides] for dilution of a drug in the diffusion space" are not taught or suggested by Wolinsky et al. in view of Aoki, et al. Applicants request that the Board overturn this rejection.

RELIEF REQUESTED

The Appellant respectfully requests that the rejection of Claims 1, 2, 4, 6-13, 19-20, 22, 24, 25, 29 and 31-33 under 35 U.S.C. § 102(b) and the rejection of Claims 21 and 30 under 35 U.S.C. § 103(a) be reversed, and that the application be remanded to the Examiner with instructions to issue a Notice of Allowance.

Respectfully submitted,

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CLAIMS APPENDIX

1. (Previously Presented) A device comprising:

an elongate body comprising a proximal end defining an inlet, and a distal end defining an outlet, the elongate body defining a lumen in the elongate body, said lumen extending between the proximal and distal ends; and

a diffuser element operatively associated with the elongate body so as to define a diffusion space, wherein the elongate body distal end outlet is disposed in and in fluid communication with the diffusion space, and wherein the diffuser element is drug-permeable and water-permeable to provide for dilution of a drug in the diffusion space.

2. (Previously Presented) The device of claim 1, wherein the diffuser element comprises a semipermeable membrane, a microporous membrane or an ion exchange membrane.

3. (Canceled)

4. (Previously Presented) The device of claim 1, wherein the distal outlet of the elongate body is defined by an exit orifice of a drug delivery device and the diffuser element is a cap in which the exit orifice is disposed .

5. (Canceled)

6. (Original) The device of claim 1, wherein the diffusion space is defined by an outer wall of the elongate body and an inner wall of the diffuser element.

7. (Previously Presented) The device of claim 1, wherein said diffuser element surrounds at least a portion of said elongate body.

8. (Original) The device of claim 1, wherein the diffuser element is microporous.

9. (Original) The device of claim 1, wherein the diffuser element is a dense membrane.

10. (Original) The device of claim 1, wherein the diffuser element is an ion-exchange membrane.

11. (Previously Presented) The device of claim 1, wherein a diffuser element distal end extends distally beyond the elongate body distal end.

12. (Original) The device of claim 1, wherein the diffuser element is a ring-shaped element.

13. (Previously Presented) The device of claim 1, wherein the diffuser element is selectively permeable to water.

14. -18. (Canceled)

19. (Previously Presented) The device of claim 1, wherein the elongate body lumen is adapted for delivery of agent at a low volume rate.

20. (Previously Presented) A drug delivery system comprising the device of claim 1 operably attached to a drug reservoir.

21. (Previously Presented) The drug delivery system of claim 20, wherein the drug reservoir contains Baclofen.

22. (Previously Presented) The drug delivery system of claim 20, wherein said drug is delivered in microliter or submicroliter quantities per day.

23. (Canceled)

24. (Previously Presented) The method of claim 25, wherein the formulation is introduced into the inlet at a low volume rate.

25. (Previously Presented) A method for delivery of an agent to a delivery site in a subject, the method comprising the steps of:

(a) implanting at the delivery site at least a distal portion of a device, the device comprising:

an elongate body comprising a proximal end defining an inlet, and a distal end defining an outlet, the elongate body defining a lumen in the elongate body, said lumen extending between the proximal and distal ends; and

a diffuser element operatively associated with the elongate body so as to define a diffusion space, wherein the elongate body distal end outlet is disposed in and in fluid communication with the diffusion space, wherein the diffuser element is drug-permeable and water-permeable so as to provide for dilution of a drug in the diffusion space and movement of drug out of the device; and

(b) introducing into the elongate body inlet a drug at a first concentration, wherein said drug moves through the elongate body lumen, out the elongate body outlet, and into the diffusion space, and further wherein water from the environment outside the device passes into the diffusion space through the diffuser element to dilute drug in the diffusion space to a second concentration, and wherein said diluted drug diffuses out through the diffuser element to exit the device at the delivery site in the subject.

26. - 28. (Canceled)

29. (Previously Presented) The device of claim 1 wherein the diffuser element comprises a polymeric film.

30. (Previously Presented) The device of claim 29 wherein the diffuser element has a Diffusion Coefficient (DC) value in the range between 4.1×10^{-6} and 3.3×10^{-5} µg/cm/sec.

31. (Previously Presented) The device of claim 1, wherein the elongate body is drug-impermeable wherein the diffuser element is substantially impermeable to drug and selectively permeable to water.

32. (Previously Presented) The method of claim 25, wherein the elongate body lumen is at least partially filled with a drug formulation prior to said implanting.

33. (Previously Presented) The device of claim 1, wherein the diffuser element is substantially impermeable to biological fluids or components of biological fluids.

EVIDENCE APPENDIX

No evidence submitted under 37 CFR §§ 1.130, 1.131 or 1.132 has been relied upon by Appellant in this Appeal.

RELATED PROCEEDINGS APPENDIX

There are no decisions rendered by a court or the Board which would directly affect or be directly affected by, or have a bearing on the Board's decision in the instant appeal.